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54 Title: USE OF α-ALKYLGLUCOSIDES AND α-ALKYLGLUCOSIDE ESTERS AS ANTIMICROBIAL EMULSIFYING AGENTS

57 Abstract

The invention discloses the use in a composition, in particular pharmaceutical, cosmetic or agri-food compositions, of an α-alkylglucoside constituent or an α-alkylglucoside ester constituent, or a mixture of both, as a microbicidal agent, in particular bactericidal or fungicidal or both, the said constituent or the said mixture being in sufficient proportion to preserve the said composition from microbial, in particular bacterial and/or fungal, development.

USE OF α-ALKYLGLUCOSIDES AND α-ALKYLGLUCOSIDE ESTERS AS ANTIMICROBIAL EMULSIFYING AGENTS

The present invention concerns the use of α-aklylglucosides and/or α-alkylglucoside esters, more particularly α-butylglucoside esters as antimicrobial agents, in particular antibacterial and/or antifungal agents for the preparation of pharmaceutical, cosmetic or food-processing compositions or other types of compositions as soon as the presence of such an agent proves to be necessary. The invention relates in addition to specific compositions for such uses and including such antimicrobial agents.

The protection of cosmetic, dermatological, pharmaceutical and food-processing products from a possible microbial development requires the use of preservatives. However, the majority of preservatives currently used, especially in cosmetics and in topical pharmaceutical specialties are capable of causing skin and eye irritation. In addition, incompatibilities with the components used, especially certain surfactants, are possible.

The fatty acid esters of sugar or of alylglucosides are known for their emulsifying and conditioning properties with respect to the hair and skin. Their use in cosmetics is described in numerous articles and patent applications.

Unexpectedly, the inventors have discovered that α-alkyl-glucoside esters have, in addition to the known emulsifying properties, bactericidal and/or fungicidal properties. In aprallel with this, it has been discovered that some alkylglucosides, some of which could constitute the substrate of the esterification reaction furnishing the said esters, also possess certain antimicrobial properties, in particular bactericidal properties.

A goal of the present invention is thus to supply means to permit the effective prevention or reduction of microbial developments in an environment which is favorable to it, while avoiding the problems inherent in the use of certain types of preservatives as mentioned above.

The present invention thus has as its principal subject the use of a composition, in particular a pharmaceutical, cosmetic or food-processing composition, of an α-alkylglucoside component or an α-alkylglucoside ester component or a mixture of the two, as a microbicidal, in particular a bactericidal or fungicidal agent or both at the same time, the said component or the said mixture being in sufficient proportion to preserve the said composition from microbial development, particularly bacterial or fungal development or both at the same time.

It is understood that the present invention likewise covers the use of mixtures of at least two different component α-alkylglucoside esters and/or α-alkylglucosides.

The preservative power of such compounds thus permits a "self-protective" effect against the microbial contamination of pharmaceutical, cosmetic, dermatological or food-processing formulations. The α-alkylglucoside esters, and in particular the α-butylglucoside esters, can be obtained by enzymatic esterification starting from an α-alkylglucoside such as is described in the patent PCT/FR92/00782. The products obtained by this procedure are stereospecific (α) and are normally monoglucosides. Because of the absence of the β-anomer in the products used according to the present invention, certain physical characteristics, such as the melting point and the solubility of the alkylglucoside are defined very precisely.

The α-alkylglucosides are preferably esterified in the C_3 then C_2 positions. This enzymatic esterification

is catalyzed by an enzyme preparation having a lipase activity. The reaction conditions make it possible either to enrich the proportion of α-alkylglucoside monoester, with esterification primarily on the C_3, or to enrich the proportion of diester, with esterification primarily at C_2 and C_3. The process used permits saturated fatty acids to be esterified just as well as unsaturated fatty acids.

Such esters are stereospecific, chemically pure and perfectly characterized. They are in addition not found mixed with secondary products, since they are obtained by a completely enzymatic synthetic process. These α-alkylglucoside esters, being in addition non-toxic and non-irritating emulsifying agents, are thus particularly suitable for cosmetic, pharmaceutical or food use.

In a preferred use in accordance with the present invention, the component α-alkylglucoside ester, α-alkylglucoside or their mixture is in a proportion of between about 0.5% and 10%, preferably between about 2.5% and 5%,by weight of the above-mentioned composition.

In addition, the α-alkylglucoside ester component is, as a bactericidal agent, in a proportion at least equal to about 3.5%, preferably 5%, of the weight of the composition.

In a preferred use, the alkyl group of the α-alkylglucoside or of the α-alkylglucoside ester is a group containing 1 to 6 carbon atoms, preferably a butyl group.

Preferably, in such a use, the α-butylglucoside ester represents at least 40%, preferably 80% by weight of the bactericidal and/or fungicidal agent.

In a particularly preferred use, the α-alkylglucoside ester is an α-butylglucoside mono- or di-caprate, an α-butylglucoside mono- or di-palmitate, or an α-butylglucoside mono- or di-cocoate.

Among the esters that can also be used may be cited the laurates, myristates, and stearates.

As described above, the inventors have also discovered the bactericidal and fungicidal properties of α-alkylglucosides. In a preferred use of the present invention, the α-alkylglucoside component is, as a bactericidal agent, in a proportion of between about 0.8% and 5% by weight of the composition and, as a fungicidal agent, in a proportion of between about 1% and 3% by weight of the composition.

Depending on the conditions under which the use according to the present invention is effectuated, it may occur that, to some extent, the microbicidal activity of the above-mentioned components varies. It is understood that in this case it is well within the capability of one skilled in the art to adapt these conditions in order to obtain the desired microbicidal effect.

The present invention likewise relates to a pharmaceutical, cosmetic or food-processing composition in which the active principle includes an α-alkylglucoside ester, an α-alkylglucoside or their mixture, in which the alkyl group contains 1 to 6 carbon atoms. Preferably, this active principle is present in an amount of 0.5% to 10%, preferably 2.5% to 5% by weight relative to the said composition.

Preferably, the alkyl group of the α-alkylglucoside and/or the α-alkylglucoside ester is a group containing 1 to 6 carbon atoms, preferably a butyl group.

In a preferred composition of the invention, the α-alkylglucoside ester is an α-butylglucoside mono- or di-caprate, an α-butylglucoside mono- or di-palmitate, or an α-butylglucoside mono- or di-cocoate.

In a particularly preferred composition, the active principle is constituted of one of the following mixtures a), b), c) and d):

a) Polyethylene glycol(30) dipolyhydroxystearate	15%
α-Butylglucoside monocaprate	48%
α-Butylglucoside dipalmitate	37%
b) Ester [sic] of polyoxyethylene and fatty alcohol	40%
Ether of polyethylene glycol(21) and stearyl alcohol	15%
α-Butylglucoside monocaprate	26%
α-Butylglucoside monopalmitate	19%
c) Ester of citric acid and glyceryl sorbitol	20%
α-Butylglucoside monocaprate	46%
α-Butylglucoside monopalmitate	34%
d) α-Butylglucoside dicocoate	48%
α-Butylglucoside monococoate	37%
α-Butylglucoside monopalmitate	15%

These mixtures a), b), c), and d) have respectively been named BEC 4, BEC 721985, BEC SCS, and BEC SH

More preferably, the pH of a composition according to the invention is between 3 and 10, preferably approximately equal to 5.

The present invention also relates to a process for preparing an α-butylglucoside ester for use according to the invention, in which the said α-butylglucoside ester is obtained by stereospecific enzymatic esterification of α-butylglucoside in the presence of a viscosity lowering agent, in particular hexane.

The present invention also relates to an external method of antimicrobial treatment, in particular in humans, in which the compounds of the α-alkylglucoside and α-alkylglucoside ester type previously described act as antibacterial and/or antifungal agents in various galenical forms.

The inventors have therefore tested the bactericidal and/or fungicidal activity of compounds of the α-alkylglucoside and α-alkylglucoside ester type so as to determine the conditions, particularly the concentrations, at which the said compounds must be used for the desired activities to be obtained. The results of these tests have been analyzed in conformity with the French Pharmacopeia, which describes a methodology for checking the efficacy of antimicrobial preservative agents in pharmaceutical preparations and establishes criteria of minimal efficacy depending on the administration routes of the medication. Thus, specific criteria are established for topical specialties that may be considered to be similar to cosmetic products in their design. The recommended significant criteria for the bactericidal and/or fungicidal efficacy of a product are:

- <u>for a bactericidal effect</u> *(Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli)*
- reduction by 3 logarithmic units in 14 days relative to the initial population,
- no increase in microbial growth after 14 days and up to 28 days, the date of the end of the test;

- <u>for a fungicidal effect (yeasts and molds)</u> *(Candida albicans, Aspergillus niger)*
- reduction by 1 logarithmic unit in 14 days relative to the initial population,
- no increase in microbial growth after 14 days and up to 28 days, the date of the end of the test.

EXPRESSION OF RESULTS

In order to facilitate the visualization of the bactericidal or fungicidal effect of the compounds tested, the results obtained have been recorded in Figures 1 to 5 in the form of graphs showing the decrease in the number of microorganisms in logarithmic units over the course of time (1 day, 7 days, 14 days, 21 days, 28 days).

Brief description of the figures:

Figure 1 shows the antimicrobial activity of the mixture BEC 4 by representing the decrease in the number (log) of bacterial (Fig. 1A and 1B) and fungal (Fig. 1C, 1D, 1E) microorganisms at different concentrations as a function of time (days) for different strains.

Figure 2 shows the antimicrobial activity of the mixture BEC 721985 by representing the decrease in the number (log) of bacterial (Fig. 2C) and fungal (Fig. 2A and 2B) microorganisms at different concentrations as a function of time (days) for different strains.

Figure 3 shows the antimicrobial activity of the mixture BEC SCS by representing the decrease in the number (log) of bacterial (Fig. 3A) and fungal (Fig. 3B) microorganisms at different concentrations as a function of time (days) for different strains.

Figure 4 shows the antimicrobial activity of the mixture BEC SH by representing the decrease in the number (log) of bacterial (Fig. 4A) and fungal (Fig. 4B) microorganisms at different concentrations as a function of time (days) for different strains.

Figure 5 shows the antimicrobial activity of the α-alkylglucosides by representing the decrease in the number (log) of bacterial (Fig. 5A) and fungal (Fig. 5B) microorganisms at different concentrations as a function of time (days) for different strains.

The results were also repeated in the form of tables (see below) showing the logarithmic reductions obtained depending on the different bacterial or fungal strains with which the tests were carried out.

ANTIMICROBIAL ACTIVITY

The tests effectuated permitted the antimicrobial activity of certain types of compounds or of certain mixtures of compounds to be demonstrated. It is understood that the following compounds or mixtures, which constitute the active agents, do not in any way limit the scope of the use according to the present invention.

A. Antimicrobial activity of α-alkylglucoside monocaprates

Bactericidal and fungicidal properties of α-butylglucoside monocaprate (α-BG) at 3%, 3.5%, 4%, 4.5%, and 5%:

α-Butylglucoside monocaprate (3%)		Logarithmic reduction				
		1 day	7 days	14 days	21 days	28 days
Bacteria	Staphylococcus aureus	1.7	2.3	3.5	3.8	4.4
	Escherichia coli	1.4	3.6	4.0	4.3	ST
	Pseudomonas aeruginosa	1.5	2.6	3.5	3.8	4.6
Yeast	Candida albicans	1.6	2.3	3.8	4.3	4.5
Fungi	Aspergillus niger	0.5	1.7	2.6	4.3	4.2

ST = Complete sterility, disappearance of strains

α-Butylglucoside monocaprate (3.5%)		Logarithmic reduction				
		1 day	7 days	14 days	21 days	28 days
Bacteria	Staphylococcus aureus	2.4	3.3	3.9	4.3	5.1
	Escherichia coli	2.2	3.4	3.9	4.5	ST
	Pseudomonas aeruginosa	2.7	3.5	4.0	4.5	5.0
Yeast	Candida albicans	2.6	3.4	4.1	4.6	ST
Fungi	Aspergillus niger	2.3	3.4	3.5	4.3	4.6

ST = Complete sterility, disappearance of strains

α-Butylglucoside monocaprate (4%)		Logarithmic reduction				
		1 day	7 days	14 days	21 days	28 days
Bacteria	Staphylococcus aureus	3.3	3.7	4.3	4.6	ST
	Escherichia coli	2.3	3.4	4.4	5.0	ST
	Pseudomonas aeruginosa	2.9	4.9	ST	ST	ST
Yeast	Candida albicans	2.2	3.4	4.2	4.7	ST
Fungi	Aspergillus niger	2.5	3.4	3.7	4.4	4.9

ST = Complete sterility, disappearance of strains

α-Butylglucoside monocaprate (4.5%)		Logarithmic reduction				
		1 day	7 days	14 days	21 days	28 days
Bacteria	Staphylococcus aureus	3.5	3.9	5.2	ST	ST
	Escherichia coli	2.4	3.6	4.8	4.8	ST
	Pseudomonas aeruginosa	3.7	4.1	4.8	ST	ST
Yeast	Candida albicans	2.4	3.5	4.6	ST	ST
Fungi	Aspergillus niger	2.5	3.5	4.1	4.5	ST

ST = Complete sterility, disappearance of strains

α-Butylglucoside monocaprate (5%)		Logarithmic reduction				
		1 day	7 days	14 days	21 days	28 days
Bacteria	Staphylococcus aureus	3.5	4.8	ST	ST	ST
	Escherichia coli	2.3	3.9	4.8	4.8	ST
	Pseudomonas aeruginosa	3.8	4.6	6.2	ST	ST
Yeast	Candida albicans	2.4	3.7	4.5	5.0	ST
Fungi	Aspergillus niger	2.7	3.4	4.7	ST	ST

ST = Complete sterility, disappearance of strains

B. ntimicrobial activity of α-alkylglucoside esters

α-Alkylglucoside esters, more particularly α-butylglucoside esters, have been combined or not with other components to form the mixtures below called "BEC":

BEC 4	Polyethylene glycol(30) dipolyhydroxystearate	15%
	α-Butylglucoside monocaprate	48%
	α-Butylglucoside dipalmitate	37%
BEC	Ester [sic] of polyoxyethylene and fatty alcohol	40%
721985	Ether of polyethylene glycol(21) and stearyl alcohol	15%
	α-Butylglucoside monocaprate	26%
	α-Butylglucoside monopalmitate	19%
BEC	Ester* of citric acid and glyceryl sorbitol	20%
SCS	α-Butylglucoside monocaprate	46%
	α-Butylglucoside monopalmitate	34%

[* see also similar lists on pp. 24, 26 of original, which omit the words "Melange de" (= mixture of)]

BEC SH	α-Butylglucoside dicocoate	48%
	α-Butylglucoside monococoate	37%
	α-Butylglucoside monopalmitate	15%

The proportion of the above mixtures in the various composition is expressed in the following tables as percentage by weight relative to the said composition.

I. Antimicrobial efficacy of the mixture BEC 4

a) Bactericidal activity of the mixture BEC 4 at 3.5% and 5% by weight relative to the total composition

STAINS	1 DAY	7 DAYS	14 DAYS	21 DAYS	28 DAYS
Staphylococcus aureus	0.8	2.5	3.9	4.5	4.4
Escherichia coli	1.6	3.7	3.6	4.7	4.7
Pseudomonas aeruginosa	1.3	2.6	3.6	3.7	4.7

BEC at 3.5%

STAINS	1 DAY	7 DAYS	14 DAYS	21 DAYS	28 DAYS
Staphylococcus aureus	1.4	3.7	4.4	4.5	4.4
Escherichia coli	1.7	2.6	3.6	3.6	3.6
Pseudomonas aeruginosa	1.4	3.6	4.3	4.4	4.4

BEC 4 at 5%

In conformity with the specifications of the French Pharmacopeia, the mixture BEC 4 induced a significant bactericidal effect at 3.5%, with a logarithmic reduction of more than 3 after 14 days. This effect is accentuated for a concentration of 5%, particularly for the strains *Staphylococcus aureus* and *Pseudomonas aeruginosa.*

b) Fungicidal activity of the mixture BEC 4 at 2.5%, 3.5% and 5% by weight relative to the total composition

STAINS	1 DAY	7 DAYS	14 DAYS	21 DAYS	28 DAYS
Candida albicans	0.5	1.4	2.6	3.4	3.3
Aspergillus niger	0.7	1.0	1.5	1.5	1.4

BEC 4 at 2.5%

STAINS	1 DAY	7 DAYS	14 DAYS	21 DAYS	28 DAYS
Candida albicans	1.4	3.7	3.8	3.9	3.9
Aspergillus niger	0.5	2.4	3.3	3.3	3.3

BEC 4 at 3.5%

STAINS	1 DAY	7 DAYS	14 DAYS	21 DAYS	28 DAYS
Candida albicans	1.5	3.9	4.7	4.7	4.8
Aspergillus niger	0.5	3.4	3.5	3.5	3.6

BEC 4 at 5%

In conformance with the specifications of the French Pharmacopeia, the mixture BEC 4 induced a fungicidal effect greater than minimum requirements. This effect is accentuated, as is well known, as a function of increasing concentrations used. Thus for *Candida albicans*, the logarithmic reductions are 2.6 / 3.8 / 4.7 for concentrations of 2.5% / 3.5% / 5%, respectively. For *Aspergillus niger*, the increase in logarithmic reductions as a function of the concentration is lower: they are 1.5 / 3.3 / 3.5 for concentrations of 2.5% / 3.5% / 5%, respectively,.

II. Antimicrobial efficacy of the mixture BEC 721985

a) Bactericidal activity of the mixture BEC 721985 at 5% by weight relative to the total composition

STAINS	1 DAY	7 DAYS	14 DAYS	21 DAYS	28 DAYS
Staphylococcus aureus	1.7	2.4	3.6	4.4	4.7
Escherichia coli	0.9	1.7	3.5	3.6	3.9
Pseudomonas aeruginosa	1.5	2.9	3.5	4.4	4.7

BEC 721985 at 5%

The mixture BEC 721985 induced a significant bactericidal effect at a concentration of 5%, with a logarithmic reduction of more than 3 after 14 days.

b) Fungicidal activity of the mixture BEC 721985 at 3.5% and 5% by weight relative to the total composition

STAINS	1 DAY	7 DAYS	14 DAYS	21 DAYS	28 DAYS
Candida albicans	1.6	3.4	3.5	3.8	4.1
Aspergillus niger	0.6	2.4	2.7	3.4	3.8

BEC 721985 at 3.5%

STAINS	1 DAY	7 DAYS	14 DAYS	21 DAYS	28 DAYS
Candida albicans	0.9	1.5	2.7	3.6	3.8
Aspergillus niger	0.6	2.4	3.3	3.5	3.6

BEC 721985 at 5%

The mixture BEC 721985 induced a significant fungicidal effect starting at 3.5%. Thus for *Candida albicans*, the logarithmic reductions vary from 3.5 to 2.7 for concentrations of 3.5% and 5%, respectively. For *Aspergillus niger*, the logarithmic reductions are 2.7 and 3.3 for concentrations of 3.5% and 5%, respectively.

III. Antimicrobial efficacy of the mixture BEC SH

a) Bactericidal activity of BEC SH at 4% and 5% by weight relative to the total composition

STAINS	1 DAY	7 DAYS	14 DAYS	21 DAYS	28 DAYS
Staphylococcus aureus	1.6	4.5	4.7	5.3	5.4
Escherichia coli	1.7	4.5	4.6	5.3	4.3
Pseudomonas aeruginosa	2.1	3.4	4.7	5.3	4.6

BEC SH at 4%

STAINS	1 DAY	7 DAYS	14 DAYS	21 DAYS	28 DAYS
Staphylococcus aureus	1.6	4.4	5.0	5.2	4.5
Escherichia coli	2.1	4.7	5.2	4.4	5.2
Pseudomonas aeruginosa	2.2	3.5	4.4	4.9	4.7

BEC SH at 5%

b) Fungicidal activity of BEC SH at 4% and 5% by weight relative to the total composition

STAINS	1 DAY	7 DAYS	14 DAYS	21 DAYS	28 DAYS
Candida albicans	1.9	3.3	4.3	5.1	7
Aspergillus niger	1.0	3.5	4.3	4.8	5.2

BEC SH at 4%

STAINS	1 DAY	7 DAYS	14 DAYS	21 DAYS	28 DAYS
Candida albicans	2.3	4.5	4.5	5.1	7
Aspergillus niger	1.4	3.8	4.6	5.0	7

BEC SH at 5%

IV. Antimicrobial efficacy of the mixture BEC SCS at 4.5% and 5% by weight relative to the total composition

a) Bactericidal activity of BEC SCS

STAINS	1 DAY	7 DAYS	14 DAYS	21 DAYS	28 DAYS
Staphylococcus aureus	0.6	3.5	4.0	4.6	5.2
Escherichia coli	1.9	3.0	3.6	4.5	4.7
Pseudomonas aeruginosa	2.1	3.4	4.4	4.5	5.0

BEC SCS at 4.5%

STAINS	1 DAY	7 DAYS	14 DAYS	21 DAYS	28 DAYS
Staphylococcus aureus	1.4	3.7	4.2	4.6	5.3
Escherichia coli	2.0	4.5	5.0	4.4	5.2
Pseudomonas aeruginosa	2.2	3.4	4.0	4.8	7

BEC SCS at 5%

b) Fungicidal activity of the mixture BEC 4 at 4.5% and 5% by weight relative to the total composition

STAINS	1 DAY	7 DAYS	14 DAYS	21 DAYS	28 DAYS
Candida albicans	2.3	4.6	4.4	4.6	7
Aspergillus niger	1.5	3.4	4.2	4.7	4.4

BEC SCS at 4.5%

STAINS	1 DAY	7 DAYS	14 DAYS	21 DAYS	28 DAYS
Candida albicans	1.6	5.2	4.7	5.1	7
Aspergillus niger	1.7	3.5	4.5	4.9	4.5

BEC SCS at 5%

The incorporation of the α-butylglucoside esters into cosmetic formulations is summarized in the following table:

α-Butylglucoside	Formulation	Dosage recommended for emulsifying effect	Bactericidal activity	Fungicidal activity
BEC 4	W/O emulsion, stable, white, very smooth	2.5 - 5%	Starting at 3.5%	Starting at 2.5%
BEC 721985	O/W emulsion, stable, white, very smooth	2.5.- 5%	Starting at 5%	Starting at 3.5%
BEC SCS	O/W emulsion, stable, white, very smooth	2.5 - 5%	Starting at 3.5%	Starting at 3.5%
BEC SH	Mild hygiene products, smooth, white, stable foam	0.25 TO 0.75%	Starting at 2.5%	Starting at 2.5%

C. Antimicrobial activity of α-butylglucosides

Bactericidal and fungicidal properties of α-butylglucoside (α-BG) at 0.8%, 1%, 3% and 5% by weight relative to the total composition.

α-Butylglucoside at 0.8%)		Logarithmic reduction				
		1 day	7 days	14 days	21 days	28 days
Bacteria	Staphylococcus aureus	1.0	2.1	3.4	4.0	4.0
	Escherichia coli	1.0	2.0	2.8	3.1	3.2
	Pseudomonas aeruginosa	1.0	1.0	3.2	3.2	3.3
Yeast	Candida albicans	0.0	2.0	1.2	1.3	1.3
Fungi	Aspergillus niger	0.1	1.2	2.6	3.0	3.0

α-Butylglucoside at 1%)		Logarithmic reduction				
		1 day	7 days	14 days	21 days	28 days
Bacteria	Staphylococcus aureus	1.0	2.0	3.1	4.1	4.2
	Escherichia coli	0.0	2.1	3.5	4.1	4.2
	Pseudomonas aeruginosa	1.0	2.1	3.3	4.3	4.3
Yeast	Candida albicans	0.0	1.0	2.0	2.0	2.0
Fungi	Aspergillus niger	0.0	1.0	2.1	2.1	3.0

α-Butylglucoside at 3%)		Logarithmic reduction				
		1 day	7 days	14 days	21 days	28 days
Bacteria	Staphylococcus aureus	1.0	2.0	3.1	4.0	4.1
	Escherichia coli	0.0	2.1	3.3	4.1	4.1
	Pseudomonas aeruginosa	1.0	2.1	4.0	4.1	4.1
Yeast	Candida albicans	0.0	2.0	4.4	4.2	4.2
Fungi	Aspergillus niger	0.0	1.0	2.0	3.0	2.9

α-Butylglucoside at 5%)		Logarithmic reduction				
		1 day	7 days	14 days	21 days	28 days
Bacteria	Staphylococcus aureus	1.0	2.1	3.3	4.1	4.1
	Escherichia coli	1.0	2.1	3.2	3.3	4.1
	Pseudomonas aeruginosa	1.0	2.1	4.2	4.2	4.2
Yeast	Candida albicans	0.0	2.0	4.1	4.2	4.2
Fungi	Aspergillus niger	0.0	0.1	1.1	1.0	1.0

The counts reflected a minor diminution in the number of microorganisms for concentrations below 0.8%. α-BG corresponds to the bactericidal norms required by the French Pharmacopeia for concentrations higher than 1%. A logarithmic reduction of more than 3 was observed in the microbial count at the end of 14 days without subsequent augmentation in the count. The bactericidal activity of the α-butylglucoside used at concentrations of between 1 and 5% thus appears to be efficacious. It would seem in addition that a bactericidal effect is obtained in a first stage then a bacteriostatic effect in a second stage.

The concentrations of 1 and 3% correspond to the fungicidal norms. Surprisingly, a concentration of 5% α-BG seems less active on *Aspergillus niger* than lower concentrations. There would thus be a "dosage effect" relating to the fungicidal power of α-BG on *Aspergillus niger*.

D. Specific applications

The bactericidal and fungicidal properties make it possible to envisage the use of the α-alkylglucosides, α-alkylglucoside esters and of the "BEC" mixtures as cosmetic and pharmaceutical active principles, particularly for the following uses:

- use in the composition of products for hair hygiene and/or treatment, in particular anti-dandruff shampoos, styling products or colorants.

- use in the composition of products for skin hygiene or treatment, relating particularly to acne, in the form of a cream, milk, gel or perfumed lotion, bath or shower products, shaving or makeup products, deodorants or antiperspirants.

Conforming beauty products, care products, toiletries and hair products can in addition contain ingredients usually used in cosmetics or dermatology, such as perfumes, colorants, other preservatives, sequestering agents, vegetable, animal or synthetic oils, perfluoropolyethers, hydrating agents, anti-wrinkle agents, slimming agents, sunscreens, anionic, non-ionic, amphoteric or cationic surfactants, polymers, proteins, conditioning agents, foam stabilizers, propellants.

. Examples of compositions

The following tables show compositions including the active principles in their use according to the invention. These examples are intended to illustrate the present invention without being in any way limiting in nature.

Example 1

PHASE	INGREDIENTS	INCI NAME	%	SUPPLIER
A	BEC4		2.5	SOLABIA®
A	Lanette O	Cetostearylic alcohol	2	HENKEL ®
A	Cetiol J 600	Jojoba Oil	3.5	HENKEL ®
A	Ariamol E	PPG 15 stearyl ether	4	ICI ®
A	Ariamol 812	Capric/caprylic oil	5	ICI ®
A	DC200/350 Cs	Cyclomethicone	1	DOW
A	Cipol C_{16}	Stearylic alcohol	2.5	CORNING ®
A	Aerosil 972	Silica	0.5	HENKEL ®
A	Titanium dioxide	Titanium dioxide	10	DEGUSSA ®
A	Propylene glycol	Propylene glycol	4	
	Fucogel 1000	Biosaccharide Gum-1	5	
	Water		QSP 100	SOLABIA ®

W/O EMULSION - BEC 4/2.5%

PHASE	INGREDIENTS	INCI NAME	%	SUPPLIER
A	BEC721985		5	SOLABIA®
A	Lanette O	Cetostearylic alcohol	2	HENKEL ®
A	Cetiol J 600	Jojoba Oil	3.5	HENKEL ®
A	Ariamol E	PPG 15 stearyl ether	4	ICI ®
A	Ariamol 812	Capric/caprylic oil	5	ICI ®
A	DC200/350 Cs	Cyclomethicone	1	DOW
A	Cipol C_{16}	Stearylic alcohol	2.5	CORNING ®
A	Aerosil 972	Silica	0.5	HENKEL ®
B	Propylene glycol	Propylene glycol	4	DEGUSSA ®
B	Rhodicare %	Canthan Gum	0.15	RHONE P. ®
B	Water		QSP 100	

O/W EMULSION - BEC 721985/5%

PHASE	INGREDIENTS	INCI NAME	%	SUPPLIER
G	BEC SH		0.75	SOLABIA®
C	Miracare 2M CASE	Disodium Cocoamphodiacetate (&) Sodium lauryl Sulfate (&) sodium Laureth sulfate (&) Propylene glycol	30	RHONE P.®
B	EDTA	EDTA	0.10	
D	Dehyton K	Cocoamidopropyl Betaine	5	HENKEL ®
E	Plantarene PS10	Sodium Laureth Sulfate (&) lauryl Glucoside	5	HENKEL ®

PHASE	INGREDIENTS	INCI NAME	%	SUPPLIER
F	Comperian LS	Cocoamide DEA (&) Laureth 12	1	HENKEL ®
I	Citric Acid	Citric Acid	0.4	
H	Germaben II	Propylene glycol (&) Diazolidinyl Urea (&) Methylparaben (&) Propylparaben	0.45	ISP ®
A	Water		QSP 100	

FORMULATION WITH BEC SH/0.75%]

CLAIMS

1. Use in a composition, in particular a pharmaceutical, cosmetic or food-processing composition, of an α-alkylglucoside component or an α-alkylglucoside ester component or a mixture of the two, as a microbicidal agent, particularly a bactericidal or fungicidal agent or both at the same time, the said component or the said mixture being in sufficient proportion to preserve the said composition from microbial, particularly bacterial or fungal development or both at the same time.

2. Use according to claim 1, characterized by the fact that the component or mixture is in a proportion of between 0.5% and 10%, preferably between about 2.5% and 5% by weight of the said composition.

3. Use according to claim 2, characterized by the fact that the α-alkylglucoside ester component, as a bactericidal agent, is present in a proportion at least equal to about 3.5%, preferably 5%, by weight of the composition.

4. Use according to any one of the claims 1 to 3, characterized by the fact that the alkyl group of the α-alkylglucoside or of the α-alkylglucoside ester contains 1 to 6 carbon groups.

5. Use according to claim 4, characterized by the fact that the alkyl group is a butyl group.

6. Use according to claim 5, characterized by the fact that the α-butylglucoside ester represents at least 40%, preferably at least 80% by weight of the bactericidal and/or fungicidal agent.

7. Use according to any one of the claims 1 to 6, characterized by the fact that the α-alkylglucoside ester is an α-butylglucoside mono- or dicaprate, an α-butylglucoside mono- or di-palmitate, or an α-butylglucoside mono- or dicocoate.

8. Use according to any one of the claims 1 to 7, in which different α-butylglucoside ester components are combined or not with other components according to the distribution a), b), c) or d) below:

a) Polyethylene glycol(30) dipolyhydroxystearate	15%
α-Butylglucoside monocaprate	48%
α-Butylglucoside dipalmitate	37%
b) Ester [sic] of polyoxyethylene and fatty alcohol	40%
Ether of polyethylene glycol(21) and stearyl alcohol	15%
α-Butylglucoside monocaprate	26%
α-Butylglucoside monopalmitate	19%
c) Ester of citric acid and glyceryl sorbitol	20%
α-Butylglucoside monocaprate	46%
α-Butylglucoside monopalmitate	34%
d) α-Butylglucoside dicocoate	48%
α-Butylglucoside monococoate	37%
α-Butylglucoside monopalmitate	15%

9. Use according to claim 1 or 2, characterized by the fact that the α-alkylglucoside, as a bactericidal agent, is present in a proportion of between about 0.8% and 5% by weight and as a fungicidal agent in a proportion of between about 1% and 3% by weight of the composition.

10. Use according to any one of the claims 1 to 9, in the composition of products for hair hygiene and/or treatment, in particular anti-dandruff shampoos, styling products or colorants.

11. Use according to any one of the claims 1 to 9 in the composition of products for the hygiene and/or treatment of the skin, relating particularly to acne, in the form of a cream, milk, gel or perfumed lotion, bath or shower products, shaving or makeup products, deodorants and anti-perspirants.

12. Pharmaceutical, cosmetic or food-processing composition in which the active principle includes an α-alkylglucoside ester, an α-alkylglucoside or a mixture of the two, in which the alkyl group contains 1 to 6 carbon atoms.

13. Composition according to claim 12, characterized by the fact that the active principle is present in a proportion of 0.5% to 10%, preferably 2.5% to 5% by weight relative to the said composition.

14. Composition according to claims 12 or 13, characterized by the fact that the alkyl group is a butyl group.

15. Composition according to any one of the claims 12 to 14, characterized by the fact that the α-alkylglucoside ester is an α-butylglucoside mono- or dicaprate, an α-butylglucoside mono- or dipalmitate, or an α-butylglucoside mono- or dicocoate.

16. Composition according to claim 12, characterized by the fact that the active principle is constituted of one of the mixtures a), b), c), and d) below:

a) Polyethylene glycol(30) dipolyhydroxystearate	15%
α-Butylglucoside monocaprate	48%
α-Butylglucoside dipalmitate	37%
b) Ester [sic] of polyoxyethylene and fatty alcohol	40%
Ether of polyethylene glycol(21) and stearyl alcohol	15%
α-Butylglucoside monocaprate	26%
α-Butylglucoside monopalmitate	19%
c) Ester of citric acid and glyceryl sorbitol	20%
α-Butylglucoside monocaprate	46%
α-Butylglucoside monopalmitate	34%
d) α-Butylglucoside dicocoate	48%
α-Butylglucoside monococoate	37%
α-Butylglucoside monopalmitate	15%

17. Composition according to any one of the claims 12 to 16, characterized by the fact that its pH is between 3 and 10, preferably equal to about 5.

18. Process for preparation of an α-butylglucoside ester for use in accordance with any one of the claims 1 to 11, characterized by the fact that the said α-butylglucoside ester is obtained by stereospecific enzymatic esterification of α-butylglucoside in the presence of a viscosity-lowering agent, in particular hexane.

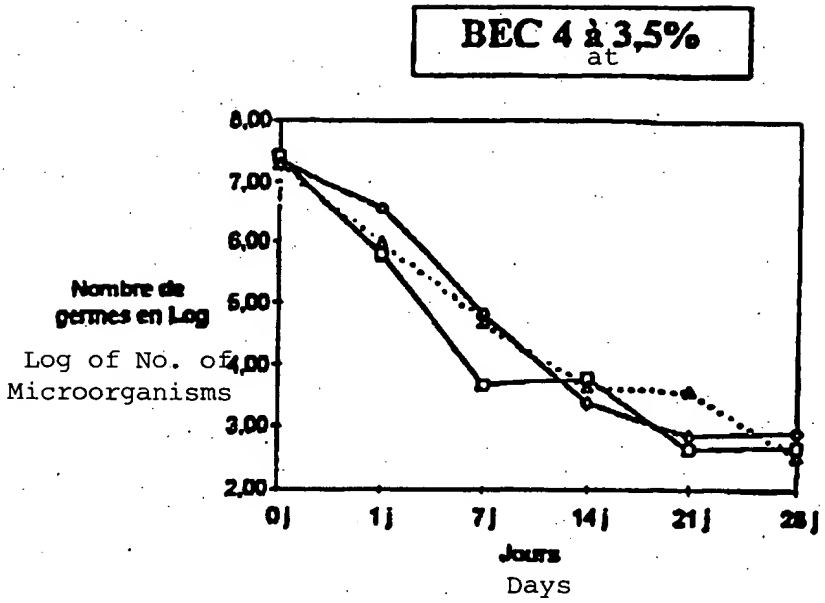

FIGURE 1A

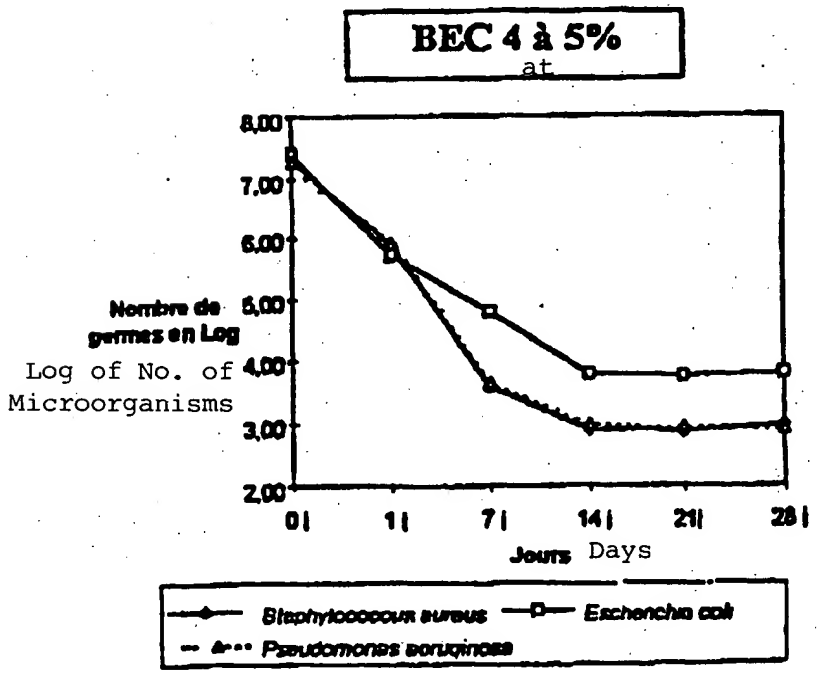

FIGURE 1B

BEC 4 à 2,5% at

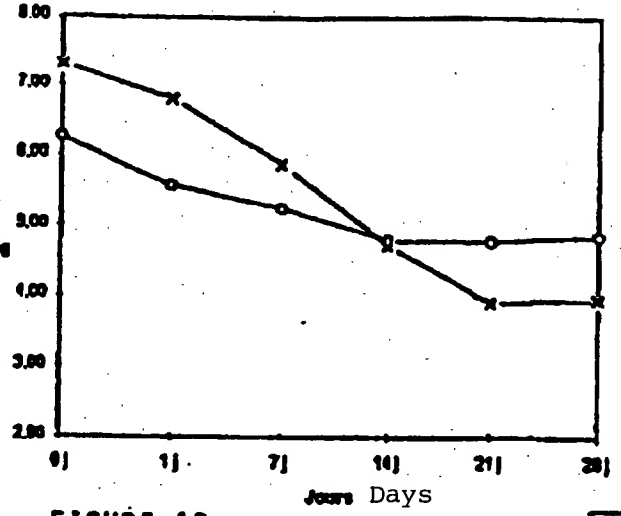

FIGURE 1C

BEC 4 à 3,5% at

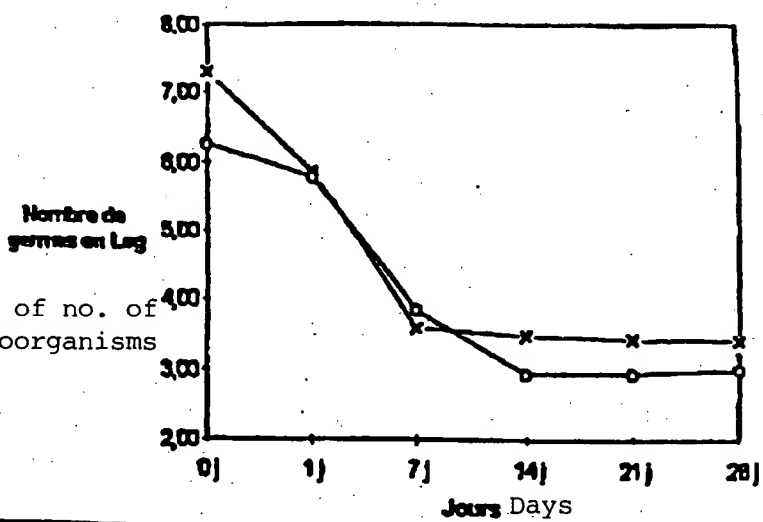

FIGURE 1D

BEC 4 à 5% at

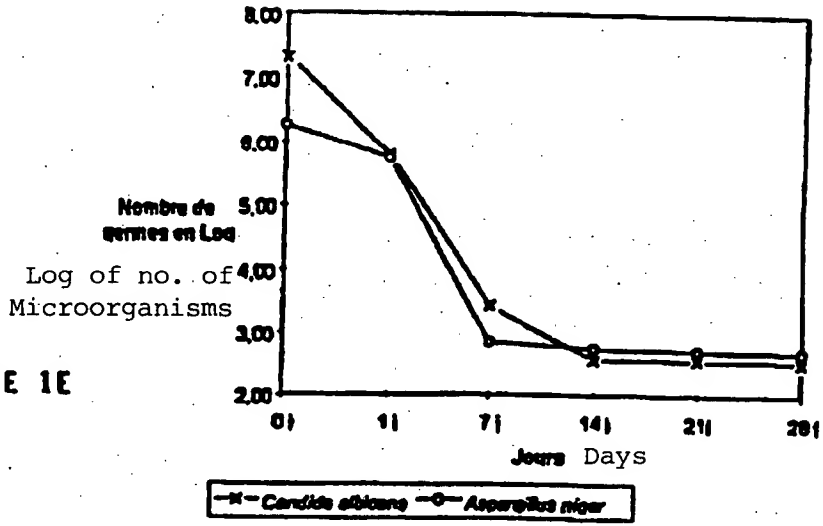

FIGURE 1E

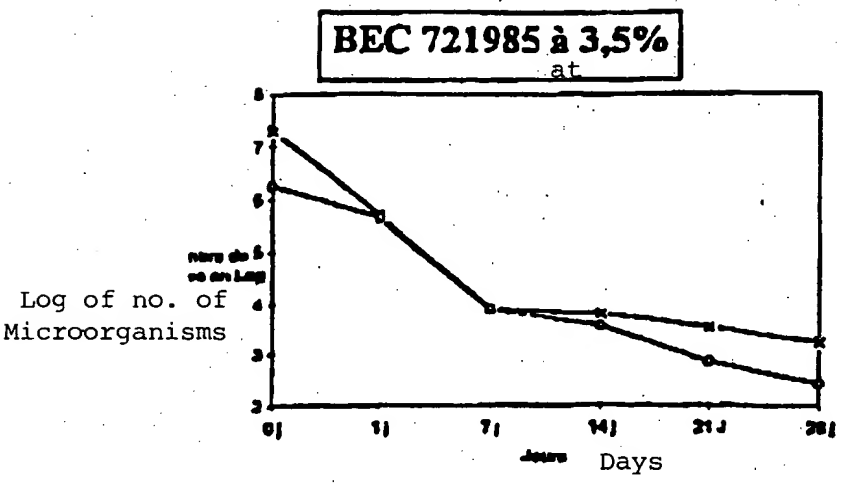

FIGURE 2A

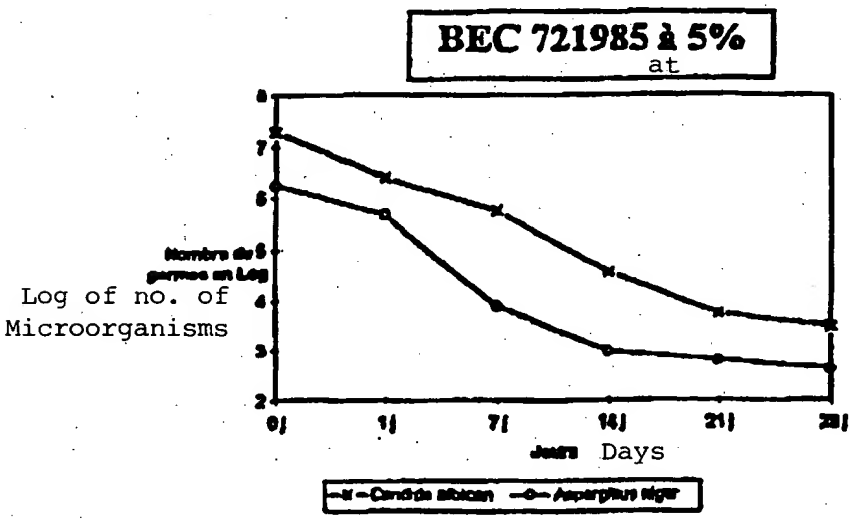

FIGURE 2B

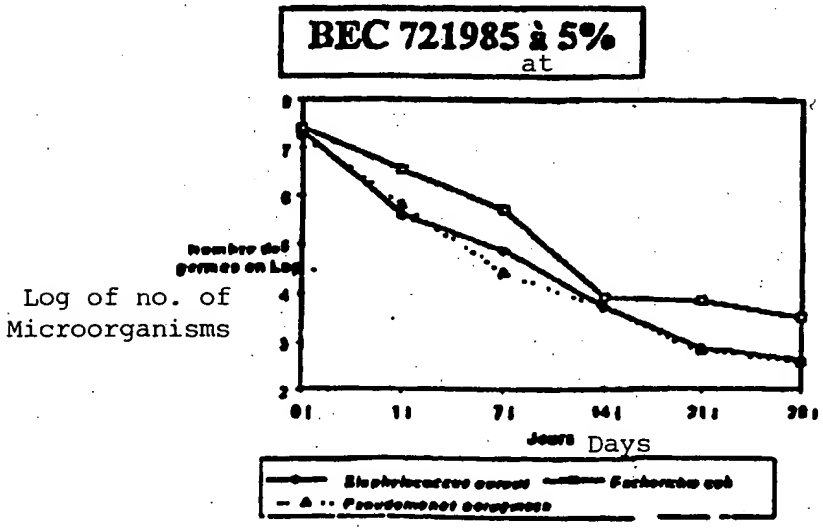

FIGURE 2C

BACTERICIDAL ACTIVITY OF BEC

ACTIVITE BACTERICIDE DU BEC SH

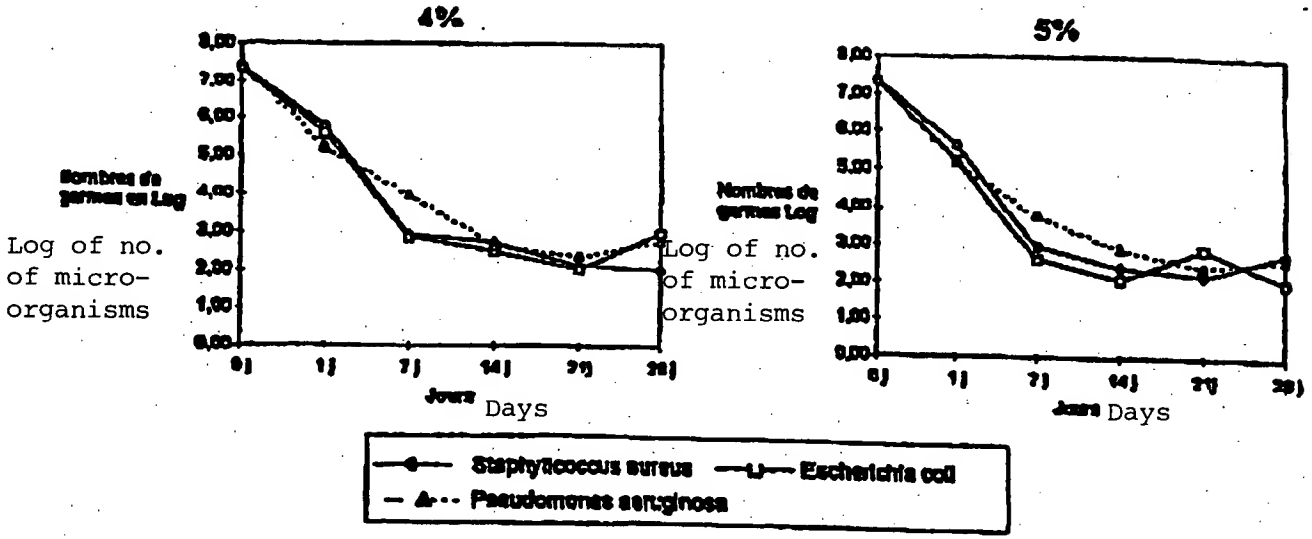

FIGURE 3A

FUNGICIDAL ACTIVITY OF BEC

ACTIVITE FONGICIDE DU BEC.SH

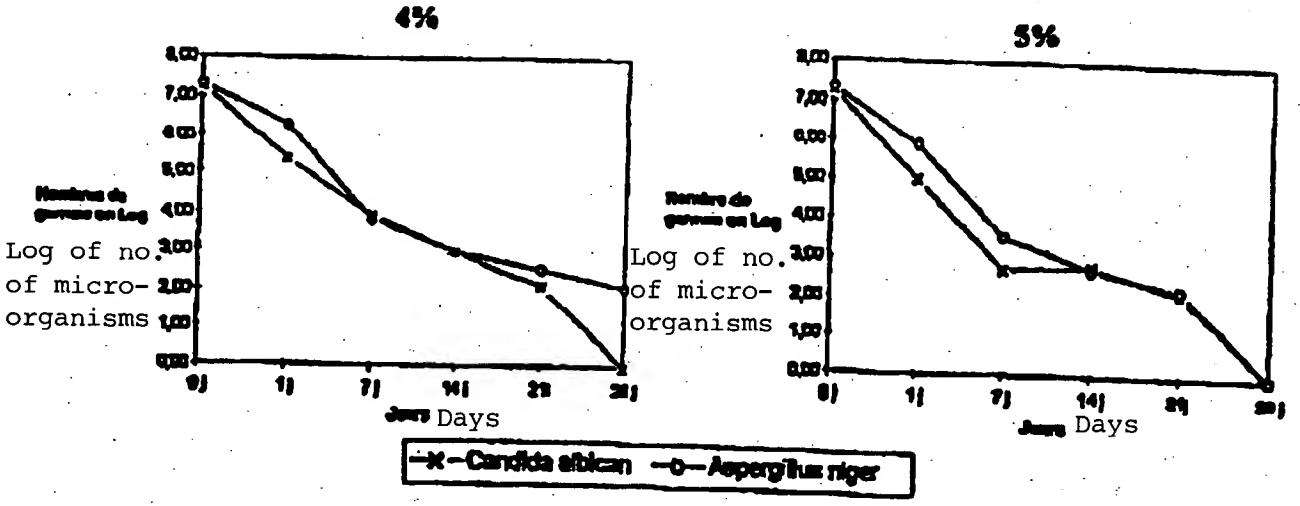

FIGURE 3B

BACTERICIDAL ACTIVITY OF BEC

ACTIVITE BACTERICIDE DU BEC SCS

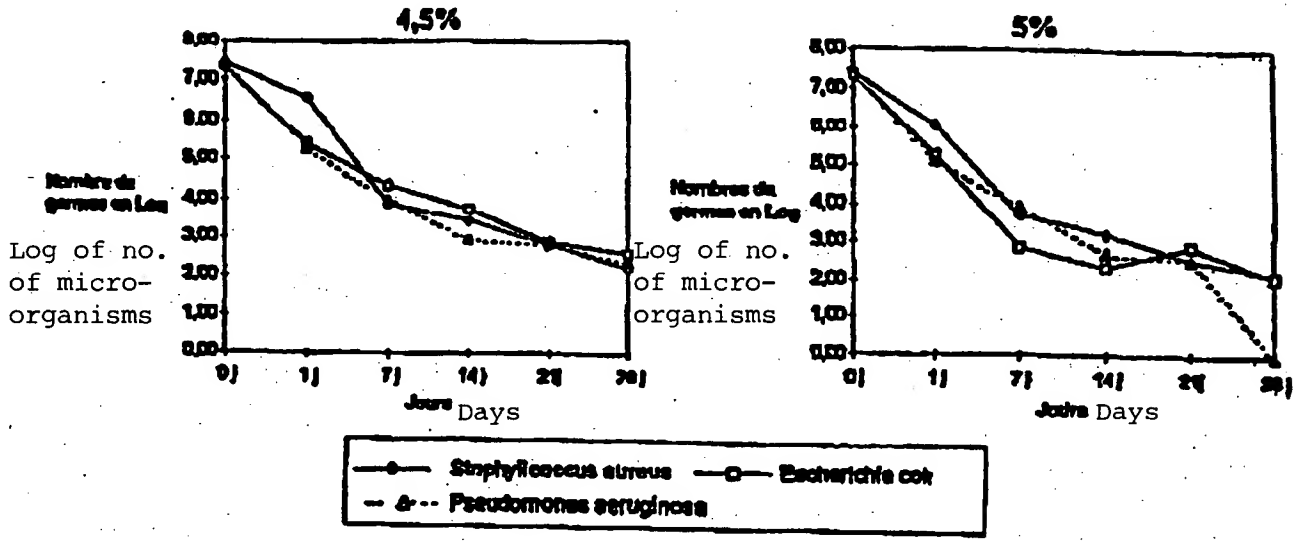

FIGURE 4A

FUNGICIDAL ACTIVITY OF BEC

ACTIVITE FONGICIDE DU BEC SCS

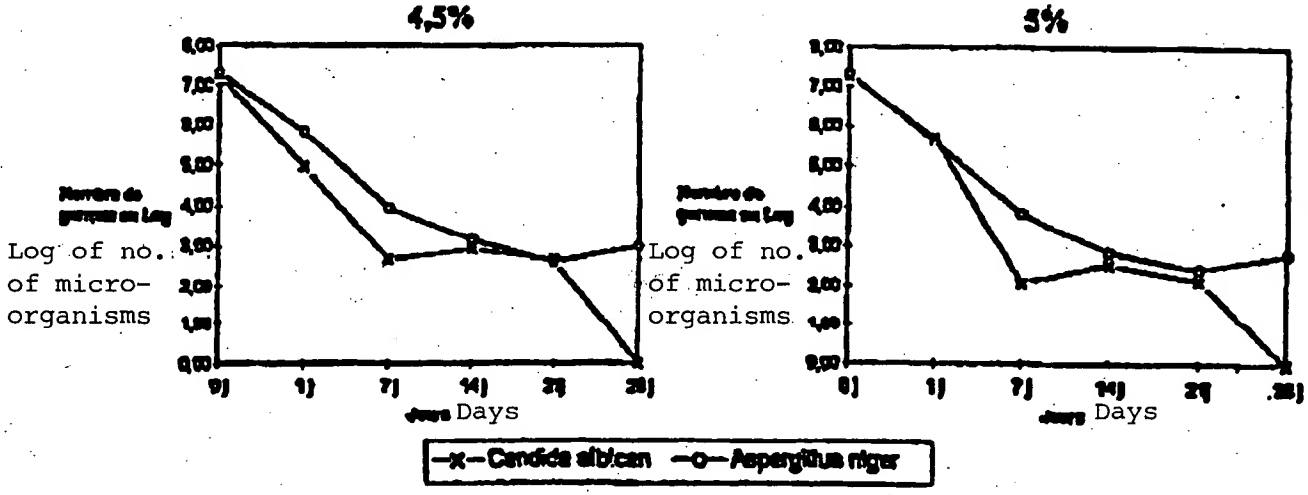

FIGURE 4B

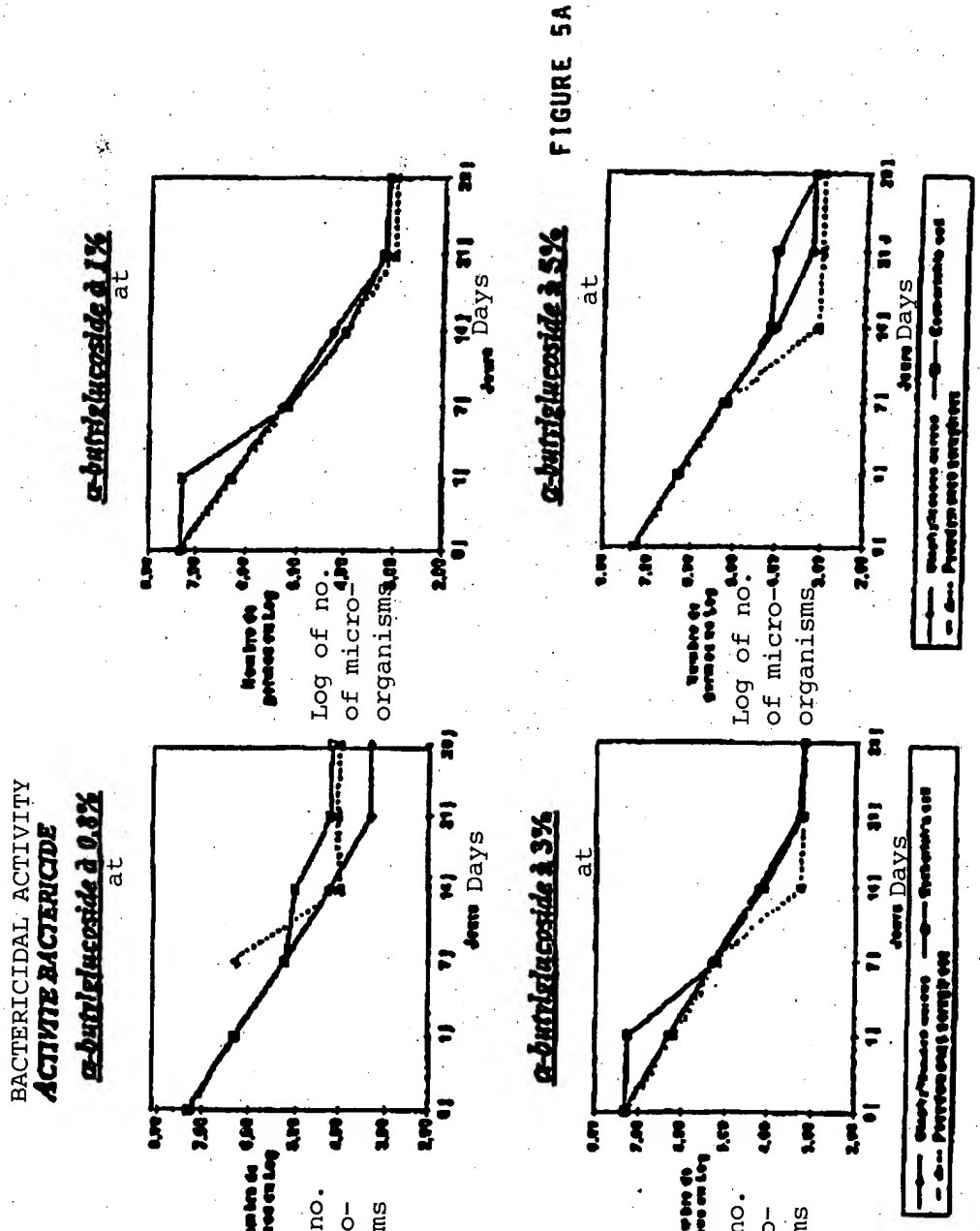
BACTERICIDAL ACTIVITY
ACTIVITE BACTERICIDE
α-butylglucoside à 0.8% at
α-butylglucoside à 1% at
α-butylglucoside à 3% at
α-butylglucoside à 5% at
Log of no. of micro-organisms
Days
Jours

FIGURE 5A

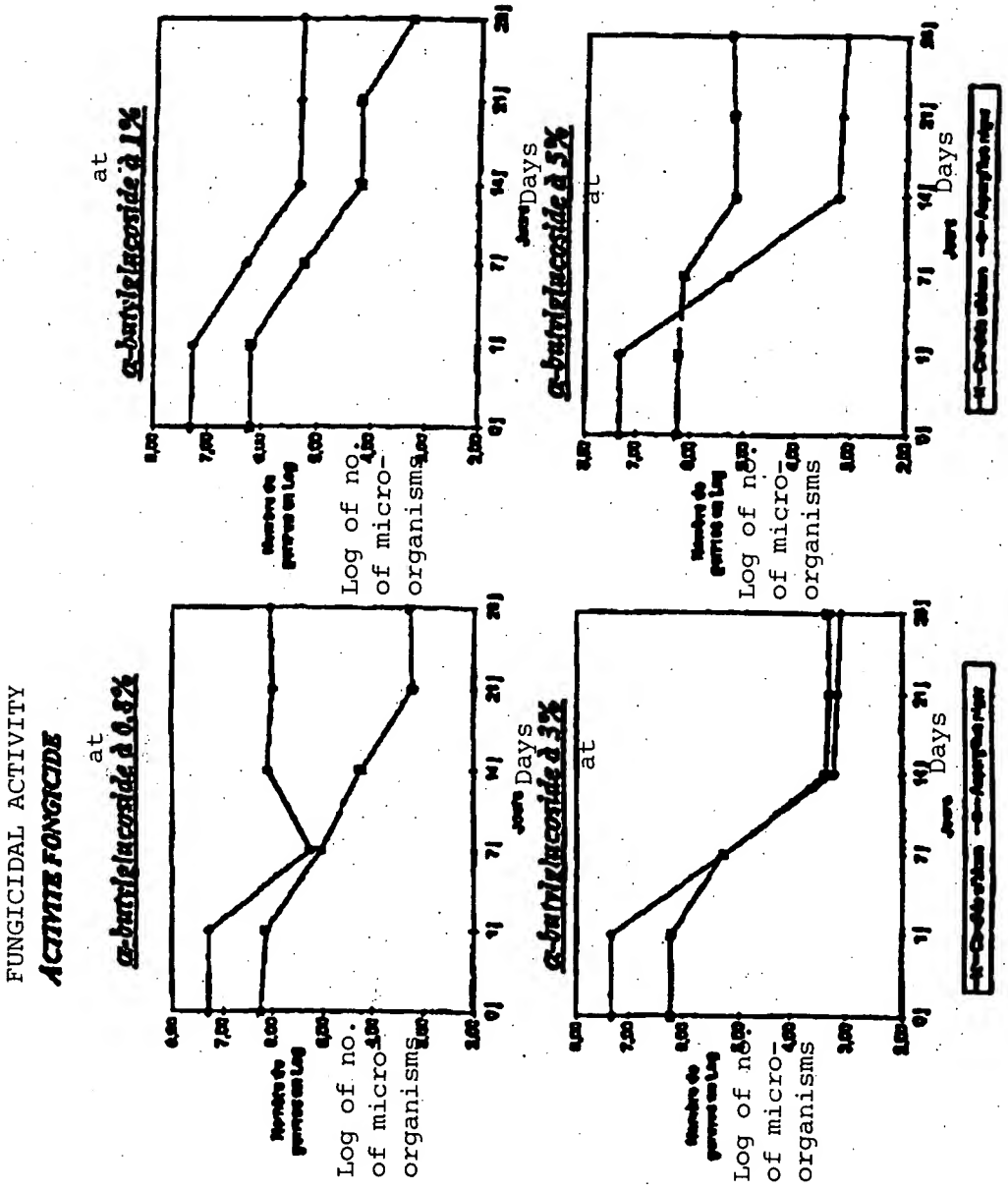
FUNGICIDAL ACTIVITY
ACTIVITE FONGICIDE
α-butylglucoside à 0.5%
α-butylglucoside à 1%
α-butylglucoside à 3%
α-butylglucoside à 5%
at
Days
Log of no. of micro-organisms

FIGURE 5B

INTERNATIONAL SEARCH REPORT

Intern al Application No
PCT/FR 97/00913

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K7/50 A23L3/3562 A01N31/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K A23K A23L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	J. AM. OIL CHEM. SOC., vol. 67, no. 12, December 1990, ILLINOIS, pages 996-1001, XP000644758 SHUICHI MATSUMURA ET AL.: "SURFACE ACTIVITIES, BIODEGRADABILITY AND ANTIMICROBIAL PROPERTIES OF n-ALKYLGLUCOSIDES, MANNOSIDES AND GALACTOSIDES." see page 996, left-hand column, paragraph 2 see page 997, left-hand column, line 9 - line 24 ---	1
A	WO 94 12259 A (ICI PLC ;HOORNE DIRK (BE); AUDA MAHROUSSA (BE)) 9 June 1994 see page 1, line 1 - line 23 see page 2, line 31 - page 3, line 31 --- -/--	1,4

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
15 August 1997	27.08.97

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016	McConnell, C

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Intern al Application No
PCT/FR 97/00913

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 255 041 A (HENKEL KGAA) 3 February 1988 see page 2, line 25 - line 36 ---	1
A	EP 0 334 498 A (CERESTAR HOLDING BV) 27 September 1989 see column 3, line 43 - line 47; claims ---	18
P,A	FR 2 730 931 A (L'OREAL) 30 August 1996 see claims 1,8,34 see page 3, line 6 - line 14 ---	1,4,5,7, 11,18
A	FR 2 680 373 A (BIO INITIATIVES) 19 February 1993 cited in the application -----	

1